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Dukoral (*cholera vaccine, inactivated oral*)

An overview of Dukoral and why it is authorised in the EU

What is Dukoral and what is it used for?

Dukoral is a vaccine that is given by mouth to protect people against cholera, a serious disease that causes severe diarrhoea. It is used in people aged from 2 years who will be visiting areas with high risk of cholera. Cholera is caused by the bacterium *Vibrio cholerae* (*V. cholerae*), which is caught from contaminated food or water.

Dukoral should be used according to official recommendations, taking into account where cholera occurs and the risk of catching the disease.

The vaccine contains 4 different inactivated strains (types) of *V. cholerae* serotype O1, and part of a toxin from one of these strains as active substances.

How is Dukoral used?

Dukoral can only be obtained with a prescription. It is available as a liquid mixture in a bottle together with powder in a sachet. The powder is dissolved in water to make an effervescent solution and the Dukoral liquid is added to this solution before the person drinks it. Food, drink and other medicines should be avoided for 1 hour before and 1 hour after taking the vaccine.

In adults and children from 6 years of age, Dukoral is given as two doses, 1 to 6 weeks apart. Children aged between 2 and 6 years should receive three doses, with an interval of 1 to 6 weeks between each dose. The course should be completed at least 1 week before potential exposure to cholera. For continuous protection against cholera, a single booster dose is recommended within 2 years for adults and children from 6 years of age, and within 6 months for children aged between 2 and 6 years.

For more information about using Dukoral, see the package leaflet or contact your doctor or pharmacist.

How does Dukoral work?

Dukoral is a vaccine. Vaccines work by preparing the immune system (the body's natural defences) to defend the body against a specific disease. Dukoral contains small amounts of inactivated (killed) bacteria that cause cholera and a fragment of the cholera toxin called the 'B subunit'. When a person is given the vaccine, the immune system recognises the killed bacteria and the toxin fragment in the

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vaccine as 'foreign' and makes antibodies against them. If, later on, the bacteria (from contaminated food or drink) enter the gut of a vaccinated person, the antibodies will be able to prevent the bacteria and their toxin from attaching to the walls of the gut and entering the body's cells.

What benefits of Dukoral have been shown in studies?

The company presented data from the published literature as well as results of 3 main studies, involving a total of almost 113,000 people, to support the use of Dukoral. In all 3 studies, Dukoral, given as either two or three doses, was compared with placebo (a dummy vaccine). The studies took place in areas where cholera is found. The main measure of effectiveness was the 'protective effectiveness' of the vaccine, calculated by comparing the number of people in the studies who developed cholera after receiving Dukoral and after receiving placebo.

The first study involved over 89,000 people in Bangladesh and compared Dukoral with the same vaccine without the toxin and with placebo. In this study, Dukoral was made using cholera toxin extracted from cholera bacteria in place of the newer recombinant toxin. The protective effectiveness of Dukoral was 85% over 6 months. Protection lasted for 6 months in children and 2 years in adults. In adults, 2 doses of the vaccine were as effective as 3.

The other two studies compared Dukoral (containing recombinant cholera toxin) with placebo in over 22,000 people in Peru. In the first of the two studies, the protective effectiveness of Dukoral was 85% for the first 5 months. The people in the second study also received a booster dose 10 to 12 months later. The protective effectiveness of Dukoral after the booster dose was 61% during the second year of follow-up.

The company also presented information on the use of Dukoral for the prevention of a severe type of traveller's diarrhoea caused by a bacterium called 'enterotoxigenic *Escherichia coli*'. However, the information was not sufficient to support the use of Dukoral in traveller's diarrhoea.

What are the risks associated with Dukoral?

Side effects with Dukoral are not common and those that can affect up to 1 in 100 people are headache, diarrhoea, and abdominal (belly) effects such as pain, cramps, gurgling (gas) or discomfort.

Dukoral must not be used in people who are hypersensitive (allergic) to any of the active substances, to any of the other ingredients or to formaldehyde. Its use should be postponed in patients with fever or short-lived illness affecting the stomach or gut.

For the full list of side effects and restrictions of Dukoral, see the package leaflet.

Why is Dukoral authorised in the EU?

The risk of cholera for regular tourists is minor, but the European Medicines Agency considered that Dukoral could be important for certain groups, such as healthcare workers in cholera epidemics or travellers visiting areas where cholera is present. Side effects with Dukoral are uncommon and generally mild. The Agency therefore decided that Dukoral's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Dukoral?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Dukoral have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Dukoral are continuously monitored. Side effects reported with Dukoral are carefully evaluated and any necessary action taken to protect patients.

Other information about Dukoral

Dukoral received a marketing authorisation valid throughout the EU on 28 April 2004.

Further information on Dukoral can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/dukoral.

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